

REMARKS/ARGUMENTS

Status of the claims

Claims 35, 37-43, 48, 49, 52 and 53 are pending and have been examined.

Independent claims 35, 42, 43, 48 and 49 have been amended to specify that the database of step (a) comprises designations for precharacterized zinc finger proteins, the target site in step (b) is preselected, and a new zinc finger protein is designed. Support for a database comprising designations for precharacterized zinc finger proteins is provided, *e.g.*, at page 30, lines 16-17. Support for a preselected target site is provided at *e.g.*, p. 29, lines 10-11 and in the title of the application. Support for the term "new zinc finger protein (new ZFP)" is provided at, *e.g.*, p. 30, lines 13-15, wherein it is stated that the claimed methods involve "systematically using a database containing information about existing ZFPs in the design of new ZFPs for a preselected target site." In this context, the term "new" is used to contrast a zinc finger protein produced by practice of the claimed methods with existing zinc finger proteins already in the database.

Claims 48 and 49 have additionally been amended to provide internal consistency in steps (c) and (3), respectively.

Claim 52 has been amended to indicate that the output potential target site can serve as the preselected target site recited in step (b) of claim 35.

Claims 41, 42 and 43 have been amended to correct various grammatical and typographical errors. No new matter is added.

Interview Summary

A personal interview with Examiner Brusca was conducted on February 19, 2004 by co-inventor Dr. Casey Case and Sean Brennan. At the interview, the art rejections over Desjarlais *et al.* were discussed. It was pointed out to the Examiner that only a single set of nucleic acid sequences¹ was disclosed by Desjarlais, and that this single set could not simultaneously be the corresponding nucleic acid sequence recited in step (a) and the target site recited in step (b). It was further pointed out by Dr. Case that Desjarlais did not disclose a

preselected target site; rather Desjarlais assembled a protein of predetermined amino acid sequence, which bound a target site whose nucleotide sequence was determined by the predetermined amino acid sequence of the protein.

The Examiner stated that Desjarlais used a database of known zinc finger domains to predict a nucleic acid target site.

Applicants thank Examiner Brusca for his time and effort in discussing these issues.

Claim rejection under 35 USC 102.

Claims 35, 37-40, 42, 43 and 53 stand rejected under 35 USC 102(b) as anticipated by Desjarlais, as previously applied.² Applicants previously pointed out that even if it is assumed *arguendo* that Desjarlais discloses a database, as recited in step (a) of claim 35, the cited reference does not disclose any of the other steps (b), (c) and (d) in claim 35. For example, if the two target sites in Fig. 1 of Desjarlais are considered to fulfill the requirement of step (a) (providing a database), they cannot also fulfill the requirement of step (b) (providing a target sequence for design of a new zinc finger protein). Desjarlais also provides no disclosure of identifying first, second and third sets of zinc finger proteins in the database as recited in step (c) of claim 35. Perforce, Desjarlais does not disclose outputting designations and subdesignations of the zinc finger proteins in the first, second and third sets, as recited in step (d) of claim 35. The Examiner disagrees, stating that Desjarlais shows provided target sites for their methods in Figure 1, correspondence between the fingers and target sites in Figure 1 and zinc finger proteins that simultaneously bind each triplet of the target site.

Applicants maintain traverse for the reasons previously given. In particular, the Examiner has not addressed Applicants' position that he is applying the same feature of the reference as two distinct steps of the claim. That is, if the provision of a table containing two

¹ which set consists of only two sequences

² The Examiner's comment that the claims are drawn to methods of designing and synthesizing a zinc finger protein comprising three zinc fingers is an oversimplification. Some of the claims (e.g., claims 42-43) specify that the designed zinc finger comprises first and second zinc fingers. Some claims e.g., claims 53, specify design but not synthesis of a zinc finger protein.

target sites is considered to fulfill the requirement of step (a) of claim 35 for providing a database, then it cannot also fulfill the requirement of step (b) of providing a target sequence. Two separate steps in a claim cannot be anticipated by one and the same action disclosed by a reference.

The claims as amended are distinguished for still additional reasons. The claims now specify design of a new zinc finger protein. The two zinc finger proteins shown in Fig. 1 of Desjarlais are both part of the database (insofar as Fig. 1 of Desjarlais can be considered to be a database). Desjarlais does not disclose designing a new zinc finger protein (*i.e.*, a zinc finger protein that is different from the zinc finger proteins in the database).

The claims also specify that the target site used for design of a zinc finger protein is preselected. By contrast, as was discussed in the interview, Desjarlais designs his zinc finger proteins first and then predicts, and finally tests, what target sites they bind to. Thus, the target sites of Fig. 1 in Desjarlais are not preselected target sites as required by amended claim 35. Claims 37-40, 42, 43 and 53 are distinguished for at least the same reasons.

Finally, Applicants note that claims 48, 49 and 53 are directed to computer-implemented methods of designing a zinc finger protein. Inasmuch as Desjarlais contains no disclosure of any type of computer-generated method, it fails to anticipate claims 48, 49 and 53.

Claim Rejections under 35 USC 103

Claims 48 and 49 stand rejected as obvious over Desjarlais, for reasons of record. Applicants respectively traverse, particularly insofar as the rejection might be applied to the amended claims.

Claims 48 and 49 are distinguished over Desjarlais for reasons analogous to those for which claim 35 is not anticipated by this reference. No secondary reference has been cited to compensate for the aforementioned deficiencies of Desjarlais. In addition, it was not obvious to use a computer to automate Desjarlais method because Desjarlais does not disclose any discrete steps in forming or using a database that would be amenable to computerized automation. As noted above, Desjarlais merely tabulates two zinc finger proteins and their predicted target sequences, and then shows binding of the zinc finger proteins to those sequences. It is not

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apparent what role computer automation would have in this process. In the office action, the Examiner merely repeats the general assertion that it is obvious to automate a process, without providing a motivation to automate the processing of a "database" containing two members, and without addressing the substance of applicant's position that Desjarlais does not disclose any process steps to automate. For this reason as well as those discussed in connection with claim 35, withdrawal of the rejection is respectfully requested.

Double patenting

It is noted that the double patenting rejections have been withdrawn based on the patentable distinctness of claims. Applicants disagree with the Examiner's comments regarding inapplicability of 35 USC 121 to claims 41 and 52 in light of Geneva Pharmaceuticals, Inc. vs. GlaxoSmithKline PLC. However, this issue is moot in view of the withdrawal of the rejection.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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